and $Xaa_2$ is an amino acid selected from the group consisting of Met, Ile, Thr or Cys and $Xaa_3$ is absent or between one and seven amino acids linked to a functional moiety.

a5 cont

40. (new) The polypeptide of claim 39 wherein the functional moiety is a cytotoxic agent.

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REMARKS

Applicants have requested the cancellation of claims 11-20 and the addition of new claims 39 and 40. The amendments to the claims are to form and are fully supported by the specification and claims as filed. Support for new claims 39 and 40 can be found at, for example, page 5, lines 10-28 of the specification. Upon entry of the instant amendment, claims 1-10, 21-38, 39 and 40 will be pending in this application.

The Requirement to Elect a Species

In the Action dated June 20, 2001, the Office stated that the present application contains claims directed to numerous distinct species of invention and has required restriction under 35 U.S.C. § 121 to a single disclosed species. (Paper 5, page 2). The Office has required that Applicants elect a single species of peptide and a single amino acid sequence and the DNA encoding the sequence for prosecution on the merits.

Applicants provisionally elect SEQ ID NO: 14 with traverse. The sequence is encompassed within presently pending claims 1-8, 21-38, 39 and 40.

Applicants respectfully request reconsideration and withdrawal of the requirement for restriction. Applicants amended pending claims relate to a peptide containing a common sequence motif.

While individual peptide sequences may or may not be considered distinct inventions by the Office, claims encompassing the motif can be examined in a single application without an undue burden on the Office.

For the foregoing reasons Applicants request that the requirement for restriction be withdrawn and the application examined on the basis of the presently pending claims without restriction.

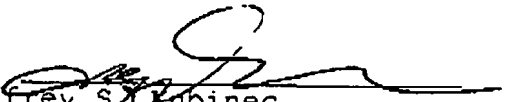
Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with Markings to show changes made**".

CONCLUSION

Applicants respectfully request that the foregoing amendments be considered and entered in the file history of the above-identified application. It is submitted that all grounds for rejection have been removed and the claims are now in condition for allowance. It is therefore earnestly solicited that such a final favorable disposition is made. The Examiner is invited to telephone Jeffrey S. Kubinec, (Reg. No. 36,575 ) at (650) 225-8228 if deemed helpful to clarify and advance prosecution.

Respectfully submitted,
GENENTECH, INC.

Date: November 15, 2001

By: 
Jeffrey S. Kubinec
Reg. No. 36,575
Telephone: (650) 225-8228

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (amended) A non-naturally occurring peptide ligand which competes for binding HER2 in an in vitro assay with a peptide ligand having the formula:

$Xaa_1$-Cys-$Xaa_2$-Gly-Pro-Gly-Cys-$Xaa_3$

[$Xaa_{(1-14)}$-Cys-$Xaa_{15}$-Gly-Pro-Gly-Cys-$Xaa_{(21-27)}$] (SEQ ID NO:90) wherein $Xaa_1$ [$X_{(1-14)}$] is absent or between one and fourteen amino acids; $Xaa_2$ [Xaa16] is an amino acid selected from the group consisting of Met, Thr, Cys and Ile and $Xaa_3$ [Xaa(21-27)] is absent or between one and 7 amino acids.

2. (amended) The peptide ligand of claim 1 having the following formula:

$Xaa_1$-Cys-$Xaa_2$-Gly-Pro-Gly-Cys-$Xaa_3$

[$Xaa_{(1-7)}$-Cys-$Xaa_9$-Gly-Pro-Gly-Cys-$Xaa_{(14-20)}$] (SEQ ID NO:92) wherein $Xaa_1$ [X(1-7)] is absent or between one and fourteen [seven] amino acids; and $Xaa_2$ [$Xaa_9$] is an amino acid selected from the group consisting of Met, Ile, Thr or Cys and $Xaa_3$ [$Xaa_{(14-20)}$] is absent or between one and seven amino acids.

3. (amended) The peptide ligand of claim 2 having the following formula:

$Xaa_1$-Cys-Ile-Gly-Pro-Gly-Cys-$Xaa_3$

[$Xaa_{(1-7)}$-Cys-Ile-Gly-Pro-Gly-Cys-$Xaa_{(14-20)}$] (SEQ ID NO:161) wherein Xaa is absent or between one and fourteen amino acids.

4. (reiterated) A peptide ligand having the formula A-A wherein A is the peptide ligand of claim 3 and "-" is an optional linker domain.

5. (amended) The peptide ligand of claim 3 having the following formula:

$Xaa_1$-Trp-Gly-Cys-Ile-Gly-Pro-Gly-Cys-$Xaa_3$

[$Xaa_{(1-5)}$-Trp-Gly-Cys-Ile-Gly-Pro-Gly-Cys-$Xaa_{(24-20)}$] (SEQ ID NO:93)

wherein $\underline{Xaa_1}$ [$Xaa_{(1-5)}$] is absent or between one and five amino acids.

6. (amended) The peptide ligand of claim 5 having the following formula:

$\underline{Xaa_1}$-Glu-$\underline{Xaa_4}$-Trp-Gly-Cys-Ile-Gly-Pro-Gly-Cys-$\underline{Xaa_{13}}$-$\underline{Xaa_6}$-Leu-$\underline{Xaa_7}$

[$Xaa_{(1-3)}$-Glu-$Xaa_5$-Trp-Gly-Cys-Ile-Gly-Pro-Gly-Cys-$Xaa_{14}$-$Xaa_{15}$-Leu-$Xaa_{(17-20)}$] (SEQ ID NO:87)

wherein $\underline{Xaa_1}$ [$Xaa_{(1-3)}$] is absent or between one and three amino acids, $\underline{Xaa_4}$ [$Xaa_5$] is an amino acid,

$Xaa_2$ is an amino acid,

$\underline{Xaa_6}$ [$Xaa_{14}$] is an amino acid,

[$Xaa_{15}$ is an amino acid] and

$\underline{Xaa_7}$ [-$Xaa_{(17-20)}$] is absent or between one and four amino acids.

7. (amended) The peptide ligand of claim 6 wherein $\underline{Xaa_1}$ [$X_{(1-3)}$-] is absent or selected from the group consisting of

Gln-Arg-Asn-

Leu-Ser-Pro-

Glu-Asn-Trp-

Ala-Ser-His-

Lys-Leu-Asn-

Thr-Gln-Ala-

Ala-Pro-Arg-

Gln-Val-Tyr-

Arg-Thr-Glu-

Phe-Ala-Gly-
Thr-Ala-Arg-
Arg-Pro-His-
Asn-Val-Cys-
Cys-Ile-Asp-
Tyr-Glu-Trp-
Arg-Trp-Asp-
His-Trp-Met-
Asn-Trp-Pro-
Phe-Asn-Trp-
Phe-Ser-Gly-
Gly-Gly-Trp-
Leu-Trp-Phe-
Gly-Ile-Pro-
Trp-Trp-Thr-
Leu-Gly-Trp-
Ser-Pro-Trp-
Arg-Gly-Trp-,

Xaa$_4$ [Xaa$_{5}$] is selected from the group consisting of:
Ala, Thr, Met, Val, Arg, Glu, Asp, Ser, Gln, Pro, Gly, Phe and Lys,

Xaa$_5$ [Xaa$_{14}$] is selected from the group consisting of:
Glu, Lys, Arg, Asp, Ser, Ala, Asn, Gly, Pro and Gln,

Xaa$_6$ [Xaa$_{15}$] is selected from the group consisting of:
Met, Phe, Ala, Met, Cys, Gln, Glu, Ala, Trp, Phe, Leu, Val, Tyr, Trp, and

Xaa$_{3,3}$ [-Xaa(17-20)] is a four amino acid peptide having the following formula:

-Xaa$_7$-Xaa$_8$-Cys-Xaa$_9$

[-Xaa$_{17}$-Xaa$_{18}$-Cys-Xaa$_{20}$].

8. (amended) The peptide ligand of claim 7 wherein -Xaa$_7$-Xaa$_8$-

Cys-Xaa$_6$ [-Xaa$_{(17-20)}$ is selected from the group consisting of:
-Gln-Ala-Cys-Met (SEQ ID NO:102)
-Leu-Gln-Cys-Trp (SEQ ID NO:103)
-Met-Ser-Cys-Val (SEQ ID NO:104)
-Leu-Arg-Cys-Ile (SEQ ID NO:105)
-Gln-Ala-Cys-Leu (SEQ ID NO:106)
-Leu-Ser-Cys-Leu (SEQ ID NO:107)
-Ile-Gly-Cys-Leu (SEQ ID NO:108)
-Leu-Ala-Cys-Leu (SEQ ID NO:109)
-Leu-Ser-Cys-Ile (SEQ ID NO:110)
-Met-Asn-Cys-Leu (SEQ ID NO:111)
-Leu-Arg-Cys-Leu (SEQ ID NO:112)
-Leu-Lys-Cys-Leu (SEQ ID NO:113)
-Leu-Gly-Cys-Leu (SEQ ID NO:114)
-Leu-Asn-Cys-Ile (SEQ ID NO:115)
-Met-Gly-Cys-Leu (SEQ ID NO:116) and
-Met-Ala-Cys-Leu (SEQ ID NO:117).

9. (amended) The peptide ligand of claim 6 wherein Xaa$_5$ [-Xaa$_{(17-20)}$] is a four amino acid peptide having the following formula

-Cys-Xaa$_6$-Xaa$_{10}$-Cys

[-Cys-Xaa$_{18}$-Xaa$_{19}$-Cys]

wherein Xaa$_6$ [Xaa$_{18}$] is an amino acid and Xaa$_{10}$ [Xaa$_{19}$] is an amino acid.

10. (amended) The peptide ligand of claim 9 wherein Xaa$_5$ [-Xaa$_{(17-20)}$] is selected from the group consisting of:
-Cys-Ala-Trp-Cys (SEQ ID NO:118)
-Cys-Ser-Trp-Cys (SEQ ID NO:119)
-Cys-Glu-Pro-Cys (SEQ ID NO:120)
-Cys-Asp-Trp-Cys (SEQ ID NO:121)
-Cys-Glu-Trp-Cys (SEQ ID NO:122)

-Cys-Asn-Trp-Cys (SEQ ID NO:123) and
-Cys-Gly-Trp-Cys (SEQ ID NO:124).

21. (amended) A polypeptide which comprises:
(a) a peptide ligand having the following formula:
$Xaa_1$-Cys-$Xaa_2$-Gly-Pro-Gly-Cys-$Xaa_3$
wherein $Xaa_1$ is absent or between one and fourteen amino acids; and $Xaa_2$ is an amino acid selected from the group consisting of Met, Ile, Thr or Cys and $Xaa_3$ is absent or between one and seven amino acids [according to any of claims 1, 4, 11, or 13] and
(b) an immunoglobulin constant region sequence.

22. (reiterated) The polypeptide of claim 21 further comprising a linker sequence.

23. (reiterated) The polypeptide of claim 20 or 21 wherein the immunoglobulin constant region sequence is the constant domain of an IgG heavy chain.

24. (reiterated) The polypeptide of claim 22 wherein said constant region sequence comprises the CH3 domain of an immunoglobulin heavy chain.

25. (reiterated) The polypeptide of claim 24 further comprising the hinge region of an immunoglobulin heavy chain.

26. (reiterated) The polypeptide of claim 25 wherein said constant region sequence comprises at least functionally active hinge, CH2 and CH3 domains of the constant region of an immunoglobulin heavy chain.

27. (reiterated) The polypeptide of claim 21 further comprising

an additional functional moiety.

28. (reiterated) The polypeptide of claim 27 wherein the additional functional moiety is selected from the group consisting of a cytotoxic agent and an enzyme.

29. (reiterated) The polypeptide of claim 27 wherein the additional functional moiety is a cytotoxic agent.

30. (amended) A pharmaceutical composition comprising a [the] peptide ligand having the following formula:
$Xaa_1$-Cys-$Xaa_2$-Gly-Pro-Gly-Cys-Xaa,
wherein $Xaa_1$ is absent or between one and fourteen amino acids; and $Xaa_2$ is an amino acid selected from the group consisting of Met, Ile, Thr or Cys and $Xaa_3$ is absent or between one and seven amino acids [of claim 1] and pharmaceutically acceptable excipient.

31. (reiterated) A pharmaceutical composition comprising the polypeptide of claim 21 and a pharmaceutically acceptable excipient.

32. (reiterated) A pharmaceutical composition comprising the polypeptide of claim 28 and a pharmaceutically acceptable excipient.

33. (reiterated) An isolated DNA molecule encoding the peptide ligand of claim 1.

34. (reiterated) The DNA molecule of claim 33 further comprising an expression control sequence operably linked to the DNA molecule.

35. (reiterated) An expression vector comprising the DNA molecule of claim 33 wherein the control sequence is recognized by a host cell transformed with the vector.

36. (reiterated) A host cell transformed with the vector of claim 35.

37. (reiterated) A method for expressing a DNA molecule encoding a peptide ligand in a host cell, comprising culturing the host cell of claim 36 under conditions suitable for expression of the peptide ligand.

38. (reiterated) The method of claim 37 further comprising recovering the peptide ligand from the culture medium.

39. (new) A composition comprising a peptide ligand having the following formula:
$Xaa_1$-Cys-$Xaa_2$-Gly-Pro-Gly-Cys-$Xaa_3$
wherein $Xaa_1$ is absent or between one and fourteen amino acids; and $Xaa_2$ is an amino acid selected from the group consisting of Met, Ile, Thr or Cys and $Xaa_3$ is absent or between one and seven amino acids linked to a functional moiety.

40. (new) The polypeptide of claim 39 wherein the functional moiety is a cytotoxic agent.